1 469 398

PATENT SPECIFICATION (11) 1 469 398

(21) Application No. 8144/72 (22) Filed 22 Feb. 1972
(23) Complete Specification filed 21 May 1973
(44) Complete Specification published 6 April 1977
(51) INT CL² A61K 7/16
(52) Index at acceptance A5B 772
(72) Inventors MELVIN GOLDMAN and JOSEPH HENRY KRONMAN

(19)

(54) DENTAL TREATMENT

(71) We, ORAL HEALTH PRODUCTS INC., a Corporation organised and existing under the Laws of the State of Delaware, United States of America, of 73 Tremont Street, Boston, Massachusetts, United States of America, do hereby declare the invention, for which we pray that a Patent may be granted to us, and the method by which it is to be performed, to be described in and by the following Statement:—

This invention relates to dental preparations and their application to the teeth for the purpose of preventing calculus, removing plaque, and removing caries.

It was found that ordinary sodium hypochlorite solutions buffered with glycine at a pH of from 9 to 11, are remarkably effective for removing plaque. Solutions at concentrations of sodium hypochlorite from 0.25—1.5% by weight were found suitable although higher concentrations are also effective, e.g., 5.25%, and not generally harmful.

It was further found that the pH can be as high as 11.5, preferably 11.1 to 11.4, and that the optimum concentration of sodium hypochlorite is 0.05 to 0.2% by weight which is less than indicated above. At a concentration of 0.1% sodium hypochlorite dissolves plaque in five seconds, caries taking somewhat longer to dissolve. In fact, concentrations as low as 0.03% or even 0.01% by weight are effective to some extent in dissolving plaque and caries.

The solutions referred to above accomplish the following objectives:

1. They dissolve carious lesions.
2. They are clinically effective in preventing caries by dissolving incipient caries as it forms.
3. They dissolve plaque.
4. As a result of dissolving plaque they prevent the development or buildup of calculus and/or caries.

The use of sodium hypochlorite in dental preparation has been proposed in the past, see e.g. U.S. Patent No. 1435498, but without recognition of the significance of maintaining the pH from 9 to 11 or to 11.5. The lower, near neutral, pH conditions previously investigated such as found in Dakin solution, are not effective in the manner herein reported in removing plaque and carious tissue.

It has also been found that in place of sodium hypochlorite, there can be used potassium hypochlorite or calcium hypochlorite. In the case of calcium hypochlorite, however, higher concentrations are required for equal effectiveness. Thus, a solution of 5% calcium hypochlorite is required to give effectiveness comparable to 0.1% of sodium hypochlorite. It is critical to use the hypochlorites specified. Other halides are ineffective as are organic chlorides.

As one preferred buffering system there is used an aqueous mixture of glycine, sodium chloride and sodium hydroxide. With this buffer there can be obtained any desired pH from 9 to 11.5. The buffer is fully disclosed, for example, in Pearse "Histochemistry Theoretical and Applied" (1968), Appendix 8, page 584.

The use of aqueous sodium hypochlorite (or potassium hypochlorite or calcium hypochlorite) by itself has the problem that it attacks the mucous lining of the mouth. and hence is not satisfactory for use with unextracted teeth.

We have already mentioned that glycine was used as a buffering agent and a preferred buffering system is an aqueous mixture of glycine, sodium chloride and sodium hydroxide, and that with this buffer there can be obtained any desired pH from 9 to 11.5.

It was then found that the ability to remove caries and dissolve plaque of the buffered solution is primarily due to the fact that N-monochloro glycine is formed *in situ* from the sodium hypochlorite (or potassium hypochlorite or calcium hypochlorite) and the glycine in the aqueous solution. N-monochloroglycine is a known material which is unstable, since it decomposes fairly rapidly.

It has further been found that on a molar basis the range of glycine to sodium hypochlorite should be from 1:1 to 15:1, preferably 7:1. (With potassium hypochlorite the molar ratio should be the same and with calcium hypochlorite there should be used twice as much glycine on a molar basis since each mole of calcium hypochlorite has two equivalents of hypochlorite.) By using at least as much

glycine as hypochlorite on an equivalent basis (e.g. mole for mole with sodium hypochlorite) there is no excess hypochlorite, e.g. sodium hypochlorite, which can attack the mucous lining of the mouth. The N-chloroglycine with or without admixture with glycine does not have an adverse effect on such lining and as stated supra is effective in dissolving plaque and removing caries.

N-monochloroglycine, with or without excess glycine, is also useful in solid or paste dentifrices at a pH of 9—11.5, usually 9—11. An inert material such as silica can be used as a thickener.

The toothpaste can contain conventional additives such as abrasive materials, sudsing agents, binders, humectants, flavouring and sweetening materials.

The abrasives preferably should be relatively water insoluble and stable at the pH ranges herein specified. They desirably should not be so abrasive as to scratch the surface of the teeth or unduly abrade the dentin, but they desirably should have just sufficient abrading power to clean the teeth. In the practice of this invention any dental abrasives can be used which have these abrasion properties.

Among the abrasives for use in the dentifrices of this invention there can be mentioned the water insoluble condensed phosphates and the water-impervious, cross-linked, thermosetting resins. Examples of such water insoluble condensed phosphates include calcium pyrophosphate, water insoluble highly polymerized calcium polyphsophate—sometimes called calcium polymetaphosphate, and water insoluble highly polymerized sodium polyphosphate—sometimes called water insoluble sodium metaphosphate. Examples of operable resin abrasives are the particulate condensation products of formaldehyde with melamine and/or urea, and others fully described in U.K. Patent 939,230. Calcium carbonate can also be used. Also there can be employed mixtures of abrasives.

The total amount of abrasive materials in dentifrices of this invention can range from 0.5% to 95% of the dry weight of the dentifrice. Usually the toothpastes contain from 20% to 60% by weight of abrasive materials.

Dentifrices conventionally contain sudsing agents. Any of the commonly used sudsing agents can be used if they are reasonably stable and form suds within the pH range of the compositions of this invention. Examples of suitable sudsing agents include, but are not limited to water-soluble salts of alkyl sulfates having from 10 to 18 carbon atoms in the alkyl group such as sodium lauryl sulfate; water soluble salts of sulfonated monoglycerides of fatty acids having from 10 to 13 carbon atoms, such as sodium coconut monoglyceride sulfonate; salts of fatty acid amides of taurine such as sodium-N-methyl-N-palmitoyl tauride; water-soluble salts of higher fatty acids, e.g., sodium stearate, potassium stearate and substantially saturated aliphatic acyl amides of saturated aliphatic monoaminocarboxylic acids having 2 to 6 carbon atoms and in which the acyl radical contains 12 to 16 carbon atoms, such as sodium-N-lauroyl sarcoside. Mixtures of two or more sudsing agents can also be used.

Sudsing agents can be used in the compositions of this invention in an amount of from 0.5% to 5.0% of the dry weight of the composition.

In preparing toothpastes, it is desirable to add some thickening material. Thickening agents include water-soluble salts of cellulose ethers such as sodium carboxymethyl cellulose and sodium carboxymethyl hydroxymethyl cellulose, natural gums such as gum karaya, gum arabic, and gum tragacanth. Colloidal magnesium aluminium silicate and finely divided silica can also be used as thickening agents for improvement in texture. Thickening agents in an amount of from 0.1% to 5.0% of the dry weight of toothpaste, can be used to form a satisfactory toothpaste.

Suitable humectants include glycerine, sorbitol, mannitol and other polyhydric alcohols. The humectants may comprise up to about 35% of the dry weight of the toothpaste composition.

Small amounts of flavourings, such as oil of wintergreen, oil of peppermint, oil of spearmint, oil of sassafras, and oil of anise can be added to the compositions of the invention as can sweetening agents such as saccharin, dextrose and levulose. Preferably flavourings are not employed if they have an adverse effect on N-monochloroglycine.

Daily rinsing of the mouth and teeth with the N-monochloroglycine solution will dissolve plaque and prevent development of its hard end product calculus. The preferred solutions at 0.1—0.2% require less time than do other proportions.

It has further been found that the compositions of the invention are effective for removing caries preliminary to filling.

In treating a decayed tooth, it is only necessary to direct a jet of the N-monochloroglycine solution against the affected area, preferably with some mechanical scrubbing with a swab. A jet of N-monochloroglycine solution may be applied from an ordinary syringe or from a mechanical pumping mechanism such as the household device commercially sold as a Water Pic, a pulsating jet. The N-monochloroglycine solution is normally prepared just before use by mixing aqueous sodium hypochlorite with aqueous glycine.

The spraying time in some instances can be reduced by treatments preceding the spraying and/or there can be incorporated a mechanical scrubbing action or other physical action in conjunction with the chemical action of the solution.

Example 1.

A decayed tooth can be prepared for filling as follows:

An 0.5 percent by weight aqueous solution of sodium hypochlorite is first prepared. To this is added about 1 percent by weight of glycine hydrochloride and sufficient sodium hydroxide (from a 1 percent by weight solution) to bring the pH to about 10 This buffered solution may be applied at room temperature or higher (preferably at body temperature) to the carious area as a jet from a commercial Water Pic. The tooth will be substantially clean of caries after a few minutes (e.g. 2—10) application. It is then dried and may be filled with amalgam in the usual manner. The molar ratio of glycine to sodium hypochlorite in this example was about 1.35 to 1.

The benefits of this invention may also be realized by incorporating the N-monochloroglycine in common dental preparations such as toothpaste and mouthwash.

Example 2.

A typical mouthwash preparation suitable for use in the practice of this invention can be prepared from:

sodium chloride	2.0 grams
sodium bicarbonate	1.0 grams
amaranth solution	2.0 cc.
peppermint water, containing 0.5% by weight sodium hypochlorite, buffered to pH 11 with glycine	240 cc.

Daily rinsing of the mouth with this solution should eliminate calculus buildup.

Example 3.

A dentifrice suitable for use in the practice of this invention can be prepared from:

calcium carbonate	33.5 grams
tricalcium phosphate	4.3 grams
glycerite of starch	31.40 grams
magnesium hydroxide	3.80 grams
white neutral soap	0.90 grams
potassium soap	0.73 grams
gum tragacanth	0.11 grams
propylene glycol	2.26 grams
flavoring (e.g. oil of peppermint)	0.80 grams
distilled water containing 1.5 percent by weight sodium hypochlorite buffered to pH 11 with glycine	20.20 grams

Daily brushing of the teeth with the above should eliminate plaque, thereby preventing the incremental buildup of calculus.

Example 4.

There was prepared an aqueous buffer solution 0.05 molar in glycine, 0.05 molar in sodium hydroxide and 0.05 molar in sodium chloride. There was also employed 1 ml. of mint flavour (A—3660 of Haarmann and Reimer). The final hypochlorite mouthwash was made by placing 500 ml. of distilled water in a 1000 ml. volumetric flask, adding the indicated amount of aqueous 5% of sodium hypochlorite solution and indicated amount of mixture of buffer and flavour (containing 1 ml. of flavour in each case). The flask was then made up to 1000 ml. The solutions prepared were as follows:

Amount of NaOCl (ml)	Moles	Concentration of NaOCl—In Product (%)	Glycine (ml)	Moles
1	.00067	0.05	98	.0049
3	.00201	0.15	96	.0048

Unless otherwise indicated in the present specification and claims, all parts and percentages are by weight.

Example 5.
Toothpaste Formulation.

	Parts
glycerine	47
water	7.3
saccharin (sodium salt)	0.04
precipitated chalk	20.8
magnesium carbonate	13.3
magnesium hydroxide	4.2
soap (powdered, neutral, white)	0.85
oil of peppermint	0.4
oil of anise	0.08
oil of spearmint	0.08
methyl salicylate	0.08
oil of caraway	0.02
distilled water containing 0.1% sodium hypochlorite buffered to pH 11.1—11.3 with glycine	5

Example 6.
Toothpowder Formulation.

	Parts
sodium chloride	44
sodium bicarbonate	24
calcium carbonate	21.5
tricalcium phosphate	5
potassium chloride	3.5
magnesium sulfate	1.75
oil of cinnamon	0.1
oil of cloves	0.07
methyl salicylate	0.08
distilled water containing 0.1% of sodium hypochlorite buffered to pH 11.2 with glycine	5

It has also been found that the pH can be as low as 8 although the range of 9 to 11.5 and especially 10.5 to 11.5 is preferred.

The free glycine can range from 0 to 14 moles per mole of N-monochloroglycine.

Aqueous sodium hypochlorite in a range of 0.01 to 5.25% by weight forms an N-monochloroglycine solution of a molar range of 0.0013 to 0.7 when glycine is added in an amount of at least 1 mole per mole of the sodium hypochlorite. Similarly aqueous sodium hypochlorite in a range of 0.25 to 1.5% by weight forms an N-monochloroglycine solution of a molar range of 0.034 to 0.17 when glycine is added in an amount of at least 1 mole per mole of the sodium hypochlorite and aqueous sodium hypochlorite in a range of 0.05 to 0.2% by weight forms an N-mono chloroglycine solution of a molar range of 0.0066 to 0.0264.

The invention provides an agent which is useful in the following methods:—

(i) a method of treating teeth in dentistry for the removal of plaque and caries, and prevention of the building up of calculus;

(ii) a method of treating teeth in dentistry which removes only plaque and caries, whilst leaving the remainder of the tooth unaffected;

(iii) a method of treating teeth in dentistry by removing plaque and caries, thus reducing the needs of mechanical removal by drills, burrs and hand tools to a minimum or eliminating them completely;

(iv) a method of treating teeth in dentistry which, even if accidentally prolonged beyond an optimum period, will remove only plaque and caries and leave the remainder of the tooth, e.g., dentine or enamel, entirely unaffected.

(v) a method of treating teeth in dentistry, for removal of plaque and caries, which is completely painless to the patient, in that it avoids vibration resulting from use of power operated tools, and pressure on sensitive portions of a tooth by hand-manipulated tools.

The brightening of teeth is a persistent goal of modern dentistry. By their nature, teeth are easily stained, and difficult to clean effectively, and it is accordingly necessary for efficient cleaning agents to be used.

Known cleaning agents, whilst being effective to clean teeth, also tend to corrode metal parts of dental appliances and fitments. For example, aqueous sodium hypochlorite has been used hitherto as a tooth brightener, but is not currently used because of its corrosive and therefore destructive effects.

The invention provides

(a) a tooth brightening agent which is effective in cleaning the teeth but is not corrosive to metal parts;

(b) an agent for use in personal hygiene, say on an everyday basis, for removing stains from the teeth, and/or preventing the build-up of stains, thereby brightening the teeth;

(c) a cleaning agent, for brightening the teeth, which can be manufactured and sold in tablet form for use in water, as a mouth-wash;

(d) a cleaning agent, for brightening the teeth, which can be produced by mixing of two solutions, at the time of use, for use as a mouth-wash.

The solutions of N-monochloroglycine should be used at a pH in the range of pH 8 to 12 and more preferably in the range of pH 10.5 to 11.5 inclusive, most preferably 11 to 11.5.

To maintain the preferred Ph range it is desirable, because hydrogen ions are generated during the decomposition of an N-halo com-

pound in aqueous solution to add a buffer system to the solution for dental or brightener treatment. Such buffer should be compatible with the N-halo compound, i.e. it should not have any deleterious effect thereon and it should be non-toxic. Borates and phosphates are examples of compatible salts for the formation of buffer systems, e.g. $Na_2B_4O_7$ can be used as the buffer since it can hold the pH above 10 even though in other systems it usually buffers at a lower pH.

The solution need only to be brought adequately into contact with the teeth for a short period to enable the plaque to be removed or to brighten teeth.

The removal may be acclerated by feeding the solution onto the affected tooth as a stream, and an erosive effect may be obtained during the course of the removal of the plaque and carious material. The erosive effect may itself be hastened by providing a pulsating stream which weakens the deposits of plaque and caries by alternate application of force followed by relaxation, resulting in mechanical fatiguing of the deposits. Also, the use of hand tool scraping helps in removing caries.

By addition of a suitable carrier, e.g., a thickening agent, such as SiO_2, to form a paste, the solution may be more readily applied with an applicator such as a toothbrush. Such a paste can be applied one or more times a day to the teeth.

Where a solution is employed it is also possible to dissolve one or more solid materials, for example in water or aqueous solution.

The teeth are then brightenend or plaque removal by simply taking a portion of the resulting solution into the mouth as a mouth wash.

In any of the materials are provided in tablet form, it is advantageous to add means for causing effervescence to increase the rate of dissolution of the tablet material(s). By way of example, equal amounts of adipic acid and sodium bicarbonate in a tablet cause effervescence upon dissolution.

Tablets in accordance with the invention may also include other materials, e.g., fillers, so long as they are compatible.

Repeated use of these solutions over a prolonged period, say 4 weeks, can be used to bring teeth up to a desired standard of brightness and to prevent build-up of plaque. Thereafter, continued daily use of the mouth wash maintains the condition of the teeth.

Unless otherwise indicated all parts and percentages are by weight.

The following solutions are illustrative of those which have been found effective:

Solutions used (Data are given in moles per liter of the water solution.)

	NaOCl	NaOH	NaCl	Amino Compound	Buffer Salt	pH*
A	0.008	0.0539	0.050	0.05 glycine	Na_2HPO_4 0.0025	11.59
B	0.008	0.0640	0.050	0.05 glycine	$Na_2B_4O_7$ 0.00125	10.77
C	0.008	0.0210	0.050	0.05 glycine	$Na_2B_4O_7$ 0.00125	9.65

* The pH value of all solutions tested remained constant within 0.2 pH units for at least one hour.

EXAMPLE I.

The following is a first example of preparation of a decayed tooth for fillings:

Solutions A, B and C were applied as a liquid stream at a temperature of 35—45°C, and preferably at body temperature circa 37°C, on a carious area of a decayed tooth. The solution was applied either at a steady pressure in the range of 10 to 100 psi., or as a pulsating jet stream where the pressure is varied from 0 to 10 psi. or from 0 to 40 psi., or from 0 to 80 psi., or from 0 to 100 psi., during one cycle at a frequency of 100 to 1500 cycles per minute through a hypodermic needle of 20 to 23 gauge. However, the pressure in either case can be increased to 200 psi.

Each tooth was substantially cleaned and ready to fill within 1 to 7 minutes, depending on the size of the cavity and its location. Judged by qualitative eye observation, the removal of caries is more effective on living unextracted teeth than on extracted teeth. A pulsating jet stream was found to be more efficient than a non-pulsating stream, even though more of the cleansing solution was used in the non-pulsating jet stream.

The following is a table showing the results obtained, using the solutions A, B and C on extracted teeth.

Caries Removal

Solution	Temp. (°C)	Needle Gauge	Frequency (c/min)	Pressure (psi)	Volume (ml)	Time for Complete Removal (min)
A	37	20	850	0–10	430	3.5
A	37	20	650	0–40	380	4.5
A	36	20	700	0–40	500	4.5
A	37	20	200	0–100	470	6.0
A	37	23	–*	40*	1150	11
B	38	20	100	0–80	480	4.5
C	37	20	1100	0–40	460	5.0
A	38	23	1500	0–100	510	7.0
A	45	20	550	0–40	570	3.5
A	35	20	800	0–80	490	1.0

* Constant non-pulsating jet stream.

A major advantage of this method of treatment, as compared to the established drilling procedure, is that even if the treatment is greatly prolonged (i.e., continued long after all the carious material is removed), no removal of or damage to healthy tooth tissue—dentine or enamel—results. This is, however, not the case if mechanical drilling is accidentally prolonged.

EXAMPLE II.

A solution for use as a mouth wash, plaque removal and tooth brightener was prepared by mixing equal volumes of aqueous hypohalite and aqueous glycine solution. The initial pH value of the glycine solution was adjusted as necessary using sodium hydroxide. A 20 ml portion of the resulting solution was taken and used to rinse the oral cavity as a mouth wash for approximately one minute. Repeated daily use brightened the subject's teeth, and maintained a desirable level of brightness and removed plaque. The quantities of all ingredients and conditions are specified in Table I, in which the hypohalite (OX^-) concentration is in percentages and all other concentrations are in Moles/l.

TABLE I

Hypohalite Solution		Nitrogen Containing Compound Solution		
		Components		Initial pH
NaOCl	0.1	Glycine	0.1	11.1
		NaCl	0.1	
NaOCl	0.1	Glycine	0.1	11.2
		NaCl	0.1	
		Na_2HPO_4	0.01	

EXAMPLE III.

The same method as given in Example II was followed except that the solution was prepared by the addition of a solid tablet of $Ca(OCl)_2$ (0.005 moles) and a tablet of glycine (0.05 moles) and $NaHCO_3$ (0.05 moles) per 1 liter of final aqueous solution.

EXAMPLE IV.

The method of Example II was followed, with the addition that each of the solutions were thickened using SiO_2 and then equal volumes of the resulting pastes were mixed and applied with a brush.

EXAMPLE V.

The method of Example II was used with the exception that the hypohalite was added as a solid ($Ca(OCl)_2$, 0.004 miles/l.) to a solution of glycine (0.05 M), NaCl (0.05 M) adjusted to a pH of 11.2.

WHAT WE CLAIM IS:—

1. A composition comprising an aqueous solution of N-monochloroglycine and buffered to a pH of 8 to 12.

2. A composition as claimed in claim 1 wherein the composition has a pH of 9 to 11.5.

3. A composition as claimed in claim 2 wherein the composition has a pH of 9 to 11.

4. A composition as claimed in claim 2 wherein the composition has a pH of 10.5 to 11.5.

5. A composition as claimed in claim 4 wherein the composition has a pH of 11 to 11.5.

6. A composition as claimed in claim 2 or claim 3 wherein the N-monochloroglycine is prepared *in situ* from sodium, potassium or calcium hypochlorite and glycine.

7. A composition as claimed in claim 6 wherein the buffer system is glycine, sodium chloride and sodium hydroxide.

8. A composition as claimed in claim 6 or claim 7 wherein the N-monochloroglycine is prepared *in situ* from sodium hypochlorite or potassium hypochlorite and glycine in a molar ratio of glycine to hypochlorite of 1:1 to 15:1.

9. A composition as claimed in claim 8 wherein the molar ratio is 7:1.

10. A composition as claimed in claim 6 or claim 7 wherein the N-monochloroglycine is prepared *in situ* from calcium hypochlorite and glycine in a molar ratio of glycine to hypochlorite of 2:1 to 30:1.

11. A composition as claimed in claim 10 wherein the molar ratio is 14:1.

12. A composition as claimed in any one of the preceding claims wherein the composition has a molar concentration of N-monochloroglycine of 0.0013 to 0.7.

13. A composition as claimed in claim 12 wherein said molar concentration is 0.0066 to 0.0264.

14. A composition as claimed in claim 12 wherein said molar concentration is 0.034 to 0.17.

15. A composition as claimed in any one of the preceding claims wherein there is present glycine in an amount of up to 14 moles per mole of N-monochloroglycine.

16. A composition as claimed in any one of claims 1 to 6 or any one of claims 7 to 15 when not appendant to claim 7 wherein the buffer is an alkali metal phosphate or borate buffer.

17. A composition as claimed in claim 16 wherein the buffer is disodium hydrogen phosphate.

18. A composition as claimed in claim 16 wherein the buffer is $Na_2B_4O_7$.

19. A composition as claimed in any one of the preceding claims wherein the composition is an aqueous solution formed by addition of one or more tablets to water or an aqueous solution.

20. A composition as claimed in claim 19 wherein at least one of said tablets effervesces on addition to said water or aqueous solution.

21. A composition as claimed in any one of the preceding claims in the form of a jet stream.

22. A composition as claimed in claim 21 wherein the jet stream is pulsating.

23. A composition as claimed in any one of claims 1 to 18 in the form of a solid or paste dentifrice.

24. A composition as claimed in claim 23 including a water-insoluble and stable abrasive.

25. A composition as claimed in claim 24 wherein the abrasive constitutes 0.5 to 95% by weight of the dry weight of the dentifrice.

26. A composition as claimed in claim 25 wherein the abrasive constitutes 20 to 60% by weight of the dry weight of the dentifrice.

27. A composition as claimed in any one of claims 23 to 26 comprising 0.1 to 5.0% by weight of the dry weight of the dentifrice of a thickening agent.

28. A composition as claimed in claim 27 wherein the thickening agent is silica.

29. A composition as claimed in any one of claims 23 to 28 comprising a sudsing agent, humectant, and/or flavouring and/or sweetening materials.

30. A composition as claimed in any one of claims 1 to 20 in the form of a mouthwash.

31. A composition as claimed in claim 1 and substantially as hereinbefore described in any one of the Examples.

For the Applicants:
CHATWIN & COMPANY,
Chartered Patent Agents,
253, Gray's Inn Road,
London WC1X 8QX.

Printed for Her Majesty's Stationery Office by the Courier Press, Leamington Spa, 1977.
Published by the Patent Office, 25 Southampton Buildings, London, WC2A 1AY, from which copies may be obtained.